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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,432	10/27/2003	Kathleen C.M. Campbell	SIU 7399	8934

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SENNIGER POWERS ONE METROPOLITAN SQUARE 16TH FLOOR ST LOUIS, MO 63102		

EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
12/20/2007	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/694,432

Applicant(s)

CAMPBELL, KATHLEEN C.M.

Examiner

Leslie A. Royds

Art Unit

1614

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 04 December 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1-9, 11-13, 15-25 and 27-29.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_  
13. ☐ Other: \_\_\_\_\_.

Leslie A. Royds  
Patent Examiner  
Art Unit 1614

## Continuation of 3. NOTE:

Applicant's after-final amendment of 04 December 2007 will not be entered into the record because the addition of new claims 30-33 clearly raises new issues that require further consideration and/or search.

In particular, the after-final amendment proposes the addition of new claims 30-33, directed to a method for treating alopecia in a patient comprising exposing the patient to radiation for a time and at an intensity sufficient to result in alopecia and orally or parenterally administering to said patient an effective amount of a protective agent comprising methionine having the structure elucidated in claim 30 or a pharmaceutically acceptable salt thereof.

However, proposed independent claim 30 now requires the treatment of alopecia in a patient that is then exposed to radiation for a time and at an intensity sufficient to result in the alopecia, whereas the originally examined claims required the treatment of alopecia in a patient that was already exposed to radiation for a time and at an intensity sufficient to result in the alopecia. Accordingly, the patient population in which proposed newly added claim 30 is practiced is clearly different than that originally examined (e.g., a patient that may be exposed to radiation subsequently to treatment with the claimed methionine agent or a patient that already has been exposed to radiation and is treated with the claimed methionine agent). Additionally, the method steps required for, e.g., original claim 1, versus those required in proposed newly added claim 30 are also clearly different from one another because original claim 1 did not require the active step of exposing a patient to radiation (since the patient was already "exposed" to the radiation; note the past tense of the verb "expose") but proposed newly added claim 30 now requires exposing the patient to radiation as well as administering the protective agent. This change in claim scope would require an additional search and reconsideration of the prior art to determine additional issues under 35 U.S.C. 102 and/or 103.

Furthermore, Applicant presents these four additional claims that are clearly different in scope than the originally examined claims without cancelling a corresponding number of finally rejected claims. In view of this fact, and further in view of the fact that proposed amendment clearly raises new issues that require further search and/or consideration, particularly for prior art issues under 35 U.S.C. 102 and/or 103, the amendment also does not materially reduce or simplify the issues for appeal and is, therefore, not entered into the record.

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's request for reconsideration of the present application in light of the newly added claims and remarks proposed and presented in the after-final amendment of 04 December 2007 have been fully considered. However, in light of the fact that the proposed amendments to the claims will not be entered into the record, the accompanying remarks regarding the obviation of the previously set forth rejections are not persuasive and will not be further considered herein.

Insofar as the request for reconsideration applies to the previously pending set of claims, Applicant traverses the rejection under 35 U.S.C. 112, second paragraph, stating that the word "exposed" in claims 1 and 22 is "the passive voice" and, therefore, encompasses all "temporal relationships" between administration of the methionine protective agent and the radiation exposure such that the scenarios claimed in instant claims 2-3, 5-9 and 23-24 are not indefinite.

However, this is not persuasive. The Examiner disagrees with the allegation that the term "exposed" is the passive voice and maintains that the term is simple past tense and clearly circumscribes a patient that has already been exposed to radiation for a time and at an intensity sufficient to result in alopecia. In view of this fact, it is herein reiterated that the administration of the methionine protective agent prior to or simultaneously with radiation exposure in a patient who has already been exposed to radiation is an administration scenario that is impossible to execute. This is because it would be generally impossible to administer the methionine prior to or simultaneously with the radiation exposure if the patient has already been exposed to the radiation. Accordingly, the rejection remains proper despite Applicant's remarks to the contrary.

Applicant further traverses the rejection under 35 U.S.C. 103(a), stating that the Dye reference relates to natural hair loss, not hair loss caused by treatment with radiation. Applicant further relies upon the fact that Dye teaches a three-phase natural hair loss cycle, including an anagen phase, catagen phase and telogen phase, with a corresponding increase in follicular calcium concentration across the three phases, and alleges that there is no reference of record that would provide a reason to believe that hair loss from causes other than the natural hair cycle would also exhibit this same increased follicular calcium concentration. Applicant relies upon various references cited at pages 10-11 of the remarks in support of the assertion that radiation induced alopecia involves p53 and is not due to differences in the calcium concentration, which is involved in the natural hair cycle. Applicant further alleges that Jacobs et al. is directed to a punch graft hair transplantation approach to treating radiation-induced alopecia and would only have suggested to the skilled artisan that hair transplantation was the best treatment approach. Applicant asserts neither Dye nor Jacobs provides a reason to combine the disclosures together, since Jacobs fails to suggest a chemical solution to radiation-induced alopecia (because it teaches surgical hair transplantation) and Dye fails to provide any reason that controlling calcium concentrations in hair follicles would have affected radiation-induced alopecia.

Applicant's traversal has been fully and carefully considered in its entirety, but again fails to be persuasive. Initially, though it is noted that Applicant relies upon various references cited at pages 10-11 of the remarks in support of the allegations that radiation-induced alopecia results from a different cause than natural hair loss, Applicant has failed to provide copies of any of these references to the Office for consideration. Accordingly, Applicant's remarks regarding this difference, in the absence of the evidence that supports this allegation, are not persuasive. Please see MPEP Sect. 2145, which states, "The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)."

Accordingly, Applicant has failed to rebut the rationale and

teachings presented in the record over Dye in view of Jacobs et al.

that the efficacy of the nutrient composition of Dye, containing d,l-methionine, pantothenic acid and divalent iron, for treating natural alopecia would not also have the same, or at least substantially similar, level of efficacy in treating alopecia induced by radiation exposure, such as, e.g., patients undergoing radiotherapy for cancer (as evidenced by Jacobs et al.) due to the clear efficacy of such a composition in decreasing hair loss and slowing alopecia progression, as evidenced by Dye. In view of such, the rejection clearly remains proper for the reasons already of record, which will not be repeated herein so as not to burden the record.

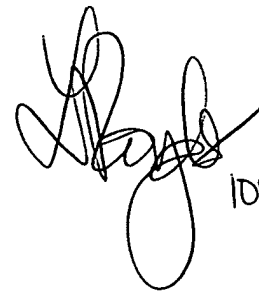
Moreover, Applicant alleges that Jacobs et al. would only have suggested to the skilled artisan to employ hair transplantation to treat radiation-induced alopecia, but fails to address the combined teachings of Dye in view of Jacob et al. as a whole. Jacobs et al. was not relied upon for its teachings of hair transplantation in patients suffering from radiation-induced alopecia, but rather was cited for its teaching that alopecia occurs in patients exposed to radiation, such as, e.g., patients undergoing radiotherapy for cancer. Applicant's focus on the discrete teachings of the cited references fails to appreciate that the references that comprise the rejection are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references that make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the combination of the cited references. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Applicant is additionally reminded that rejections under 35 U.S.C. 103(a) are based upon combinations of references, where the secondary references are cited to reconcile the deficiencies of the primary reference with the knowledge generally available to one of ordinary skill in the art to show that the differences between Applicant's invention and the prior art are such that they would have been modifications that were prima facie obvious to the skilled artisan. It is noted that the claimed invention is not required to be expressly suggested in its entirety by any one or all of the references cited under 35 U.S.C. 103(a). Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. Please also see *In re Keller*, citation supra. In view of such, arguments regarding the discrete teachings of the references without considering the combination as a whole are not persuasive.

Applicant additionally traverses the obviousness-type double patenting rejection, stating that the copending claim of the '975 application would not have suggested the instant claims because none of the claim elements would have lead an ordinary person to select alopecia and radiation from the universe of toxicities and insults claimed.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive. The '975 application explicitly names the treatment of alopecia in patients exposed to radiation for a time and an intensity sufficient to result in the alopecia. Accordingly, the need for a "suggestion" to do so from the copending claim is immaterial because the copending claim expressly teaches the same agent for the same purpose as instantly claimed and, thus, is a clear teaching to do so. Furthermore, Applicant states that the instant application was filed prior to the '975 application and that the rejection should be withdrawn when the instant case is in condition for allowance. However, in view of the fact that allowable subject matter has not yet been identified, and further in view of the absence of a Terminal Disclaimer in the record, the rejection remains proper and is maintained.

For these reasons, the claims remain properly rejected for the reasons set forth in the final rejection of September 14, 2007, of which said reasons are herein incorporated by reference.



10DEC07

*Ardin H. Marschel* 12/15/07  
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SUPERVISORY PATENT EXAMINER